

TONiC

Trajectories of Outcome in Neurological Conditions
www.finders-study.org/tonic



TONiC-MS Phase 6: Sample Collection Manual

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APPROVAL PAGE

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INTRODUCTION

This document describes the instructions for collection and shipping of samples collected from patients taking part in the TONiC-MS Phase 6 study. It also includes the Case Report Form to be collected at the same time as the samples are taken.

Protocol Title	Trajectories of Outcome in Neurological Conditions
Study acronym	TONiC Phase 6 (samples only)
REC Reference	19/NW/0536
Chief Investigator	Professor Carolyn Young
Sponsor	Walton Centre NHS Trust Lower Lane Liverpool UK L9 7LJ
Coordinating Centre	Walton Centre NHS Trust
Walton Coordinating Centre postal address	TONiC Office Sid Watkins Building 2 nd floor, Room S083 Walton Centre NHS Trust Lower Lane Liverpool L9 7LJ UK
Walton Coordinating Centre email	wcft.tonic@nhs.net
Walton Coordinating Centre telephone	0151 556 3565 0151 556 3693
Online study resources	https://www.finders-study.org/phase6
Biobank	Liverpool University Biobank
Biobank postal address	Liverpool University Biobank William Henry Duncan Building 6 West Derby Street University of Liverpool Liverpool L7 8TX
Biobank email	Biobanking@liverpool.ac.uk
Biobank telephone	0151 794 9100

CONSENT for Phases 5 and 6, +/- Phase 4

1. **Eligibility** - of the participant should already have been checked as TONiC are providing sites with lists of eligible participants each month but please do a final check confirmation prior to consenting.

The participant must fulfil the following criteria:

- i. Adult with MS capable of informed consent.
- ii. Provided with Patient Information Sheets and ICF with sufficient time to read and ask questions prior to deciding about consent. Most participants will have received these in advance as part of the DocuSign process.
- iii. Completed at least one TONiC questionnaire pack (as confirmed in lists of eligible participants for your centre supplied monthly by TONiC).
- iv. Consented with current Phase 4 ICF and PIS (if participant has not consented with current Phase 4 PIS, please consent/re-consent which can happen on day of sample collection). Phase 4 is the repeat TONiC questionnaire pack.
- v. Consented with current Phase 5 ICF and PIS (as confirmed in lists of eligible participants for your centre supplied monthly by TONiC, if participant has not consented to Phase 5 please consent which can happen on day of sample collection). Phase 5 is permission for linkage and sharing so does not require the participant to perform any activity post-consent but they must be happy for the Phase 6 genetic data to be linked to their Phase 3 +/- 4 phenotype data and shared without personal identifiers with other researchers for analysis, *including commercial partners*. The genotyping will be performed by a commercial biotechnology company so please do not take a sample if the participant declines Phase 5 as we will not be able to perform any genetic analysis if the subjects does not agree to sharing with commercial companies (see flow chart on page 9).

2. Completing informed consent for Phase 6 (and Phase 5 +/- Phase 4).

The participant should already have seen a copy of the PIS and ICF, and been able to ask questions prior to attending. Please answer any additional questions the participant may have.

Open a Biobank Sample Collection Kit (see p7), in which you will find an pre-labelled and numbered ICF plus 2 Kit Labels. Each box has a different pre-numbered Kit Label so please do not mix them up.

Put the TONiC ID number (format M####-XX) sticker in the box in the bottom left corner of the *Top* page of the carbon copy pre-numbered TONiC Phase 6 ICF included in the kit. Most participants will only sign page 1, for which a carbon copy set is available. If the patient needs page 2 please print out a paper copy of both pages from the files previously provided by TONiC and put a TONiC ID sticker on pages 1 and 2, and photocopy for *Patient* and *Records*.

The participant should initial each box according to their choices, sign and date the consent, and you should countersign. If they do not wish to donate samples for genetic research, give them the *Patient* copy, file the *Records* copy, post the *Top* copy to TONiC and the process is complete. We will contact them with more information if a non-genetic study is funded and available in future.

If the participant chooses to complete the Phase 6 consent about donating blood samples for genetic research, consenting to statements 1-9c, they are eligible for you to complete the Phase 6 case report form (CRF) and collect the biosamples using the Biobank Sample Collection Kit. Give the participant the *Patient* copy and file the *Records* copy but keep the *Top* copy handy as you will need it.

- Put one Kit number label on the Phase 6 case report form (CRF) page 11.
- There is one spare Label. Often you will return this unused in the box but we know sometimes blood tubes need to be replaced, in which case use the spare Label (see p 8).

The *Patient* and *Records* copies do not need to have labels but it does not matter if they transfer through if you had to write the TONiC number.

It is critical that you make sure that the person who signed the consent form with this Kit Label is the same person donating using the collection tubes with the same Kit Label.

COMPLETION OF PHASE 4 TONiC QUESTIONNAIRE PACK

Please provide each participant with a Phase 4 questionnaire booklet for home completion as well as SAE to return it. This should be requested of every participant, unless they have completed one in the last 8 months (any participants who have already done a recent Phase 4 pack will be indicated on the lists for your centre supplied monthly by TONiC). The default is to request completion because many sites missed posting out packs at the correct time due to understandable COVID19 issues.

COMPLETION OF PHASE 6 CASE REPORT FORM

Please write the site name (or two letter code) and add the participant's TONiC study number label (or write in their TONiC study number) on the front page of the Phase 6 CRF. You should already have put a Kit number label on page 11.

Complete the Phase 6 case report form (CRF). Instructions are included in the CRF.

Note that you can omit Section 5:DMT Record if the participant has NEVER had a MS disease modifying therapy, but all other sections should be completed.

Please ask the PI to double-check all sections highlighted in green before submission for data entry.

BIOBANK SAMPLE COLLECTION

Only open a Kit after the participant has consented to Phase 5 and Phase 6 blood for genetic analysis along with Phase 4 (p5).

Important first step: make sure you have put the participant's TONiC study number on the *Top* copy of the participant's TONiC phase 6 consent form.

The Biobank Sample Collection Kit must only be used to collect blood and urine samples from patients consented to the TONiC (phase 6) study. **This kit box has a large sticker with TONiC on it.**

Biobank Sample Collection Kit contains:



- 1 x Pre-kit Labelled ICF
- 1 x Pre-numbered kit Label for Phase 6 CRF
- 1 x spare Pre-numbered and Label
- 1 x 8.5ml SST serum collection blood tube (gold top)
- 1 x 10ml EDTA blood collection tube (purple top)
- 1 x 2.5ml Paxgene blood collection tube (red top)
- 1 x Safety-Lok blood collection set
- 1 x Urine collection pot (white top)
- 1 x TONiC Sample Information Sheet pre-numbered Label on *Top* and *Back* sheets (see Appendix 1)
- 1 x PathoShield sample bag and Box (Pre-paid for Royal Mail 1st class postage and pre-labelled with the address of the Liverpool University Biobank)
- 1 x reply-paid envelope to send the TONiC consent forms to the TONiC co-ordinating office. You **MUST** send Phase 6 consent or your samples will be destroyed.

Kit ID: Each kit has a specific Kit ID number (TON#####). Each component within the kit is labelled with this Kit ID.

One collection kit is to be used per patient per timepoint. Please make sure that you do not put a bottle from one kit in another box as that would cause quality checks to be failed and we may have to inform two participants that their kits were mixed up and their samples cannot be used due to identity uncertainty. We recommend you open and complete processing of one box at a time.

Blood Sample Collection

1. Use the tubes from the kit, pre-labelled with Kit ID number (TON#####).
2. Collect blood via venepuncture directly into the SST 8.5ml tube (gold top), EDTA 10ml tube (purple top) and Paxgene 2.5ml tube (red top).
3. Invert the gold SST tube 6 times to activate clot formation.
4. Invert the Paxgene tube and purple EDTA tube with blood in 10 times.
5. Complete the required information on part A of the TONiC Sample Information Sheet.

Urine Sample Collection

1. Request the patient collects about 15ml mid-stream urine into the urine collection pot. A primary collection can be used if required and the sample decanted into the pre-labelled collection pot.
2. Complete the required information on part A of the TONiC Sample Information Sheet.

Sample Packaging and Shipping

- Pack the 3 Blood tubes and urine pot into the PathoShield return box, using supplied tube holder and secure biohazard bag; ensure that the *Top* copy of the partially completed Biobank Sample Information Sheet is included.
- Place the PathoShield box containing samples in Royal Mail post as soon as possible.
- Do not put the TONiC Phase 6 Consent Form *Top* copy in, as that goes in the reply-paid envelope to the Walton Centre.
- Send the *Top* copy of the completed TONiC Phase 6 consent form with the Barcode Label and the participant's TONiC study number on it to the Walton Centre (see p10) by email and post (for your convenience, SAE in the collection box)*.
- Store the *Back* copy of Biobank Sample Information Sheet in the patient clinical record.

Prior to postage, blood and urine samples should be maintained at room temperature, away from direct light sources. Do NOT refrigerate blood or urine samples.

Order of blood sample collection

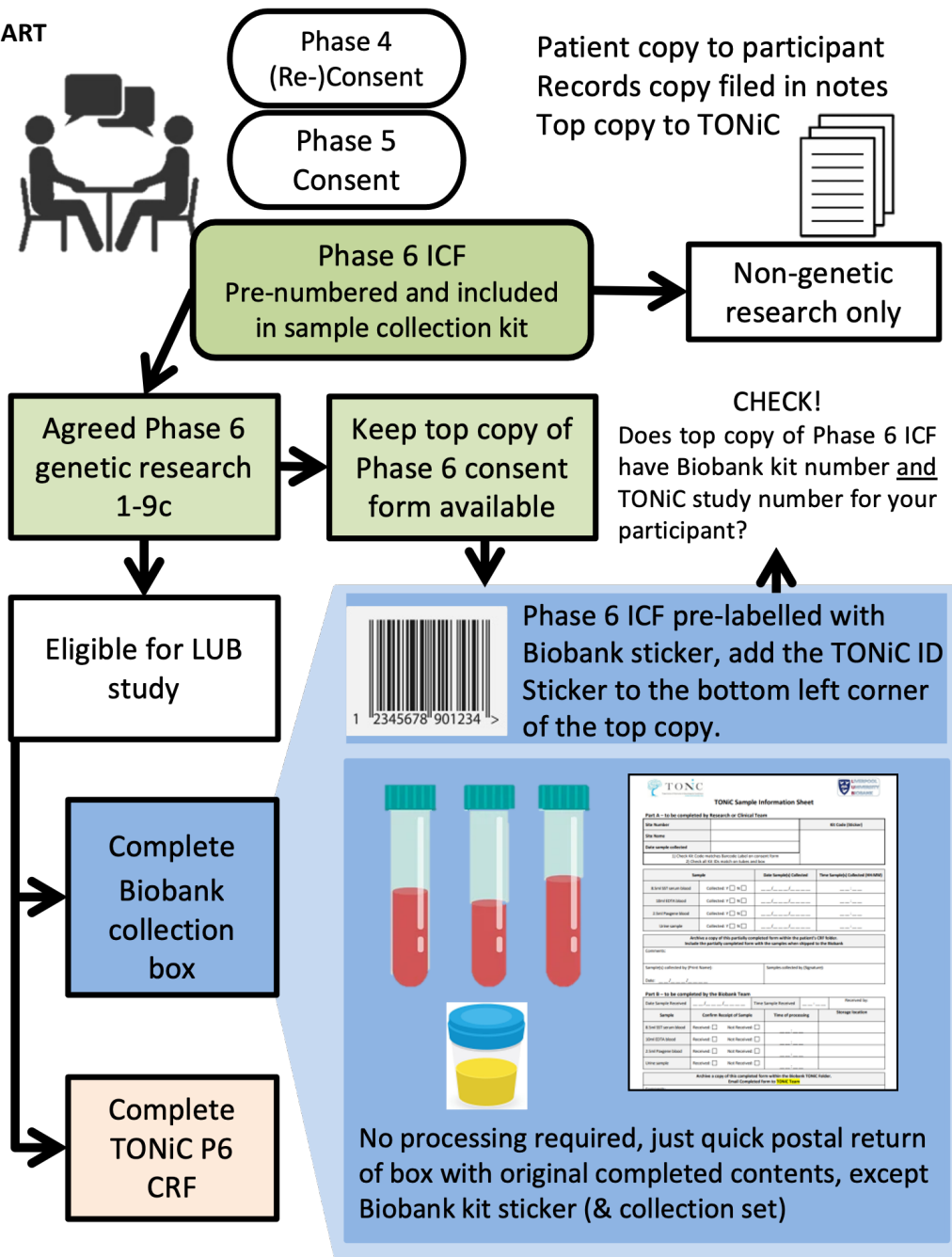
If you are taking sample for routine clinical care as well as research, take all the samples in the order you would normally follow. If you are taking samples only for research, please follow the order:



“Spoiled” blood tubes

If you need another tube because of failed vacuum on one of the supplied blood tubes, please use an EDTA or serum tube from your routine stocks and place that and the spoiled tube(s) in the box. You will not have a spare Paxgene available because this is not a routinely available tube. Use the spare Kit Label on the replacement tube. If you needed two replacement tubes, just put one unlabelled one in the box. The Biobank can work out what has occurred by seeing the new and spoiled tube(s).

FLOW CHART



What happens to:	
Filled Biobank box	Post as soon as possible to Biobank
TONiC Phase 6 ICF with study number and Biobank kit number	1. Scan and email PDF to TONiC 2. Post original top copy to TONiC
TONiC Phase 6 CRF	Send to TONiC office

*** If TONiC do not receive a signed TONiC Phase 6 consent with the Kit number Label as well as the participant's TONiC study number on it, the samples cannot be processed and we would have to ask the participant to start again with sample donation. We also cannot record an accrual or re-imburse your site's costs. Thus, please both email and post to reduce the risk of failed receipt.**

When to collect and ship samples

Please collect and post translational samples as early in the day as possible to allow for next day delivery to the Liverpool University Biobank. If at all possible, arrange blood sample collection times between Monday and Thursday to avoid deliveries over the weekend when lab staff will not be available to process samples. If samples can only be posted on Friday it may not be possible to process them for all tests (DNA should last 48 hours so if there is no other choice you can collect and post on Friday).

All blood samples will have pre-paid Royal Mail postage and should be placed in the post as soon as possible, to arrive at the Biobank within 24 hours for processing to optimise sample integrity and value. All PathoShield return boxes will be pre-labelled with the delivery address:

Liverpool University Biobank
William Henry Duncan Building
6 West Derby Street
University of Liverpool
Liverpool
L7 8TX

Where to send the TONiC Phase 6 Consent Form Top copy with the two stickers

Please email to: consents@finders-study.org

Please post to: TONiC office
Sid Watkins Building, Room S083
Walton Centre NHS Trust
Lower Lane
Liverpool
L9 7LJ

ORDERING SAMPLE COLLECTION KITS

If you are running low on kits, or they are due to expire, please request additional kits from the TONiC coordinating centre.

Sample collection packs will be shipped to sites in batches. Please report any issues with kits to the TONiC coordinating centre. If more sample collection kits are required, email the TONiC coordinating centre giving as much notice as possible to allow shipping.

RETURN OF UNUSED KITS

If you have unused kits or kit components, please contact the TONiC coordinating centre to arrange return to the LUB.

LUB, GENUITY SCIENCES AND DNA EXTRACTION AND ANALYSIS

The Liverpool University Biobank (LUB) offers a wide range of biobanking services including sample storage and processing. LUB is responsible for extracting DNA to be sent to Genuity Sciences for genotyping, and for storing the other samples so that they can be used for future healthcare research by the TONiC team and its collaborators. Genuity Sciences is a large genomics centre in Ireland with over 100 scientists processing large numbers of DNA samples per year. They will share back a copy of the genotype data with TONiC and use their copy for healthcare research. Genuity Sciences are funding the sample collection, storage and processing as well as genotyping.

Neither LUB nor Genuity Sciences can identify participants, which is why the two labels on the Phase 6 consent form are critical.

LUB CLOSE DAYS

The LUB Will be closed on the following days, please do not post samples to arrive on these days:

Friday 15 April 2022 - Good Friday

Monday 18 April 2022 - Easter Monday

Monday 2 May 2022 - May Bank Holiday

Thursday 2 June 2022 - Spring Bank Holiday

Friday 3 June 2022 – HM the Queen’s Platinum Jubilee Bank Holiday

Monday 29 August 2022 - Summer Bank Holiday

Christmas period

Monday 26 December 2022 - Monday 2 January 2023

APPENDIX 1

TONiC Phase 6 Sample Information Sheet



TONiC Phase 6 Sample Information Sheet



Part A – to be completed by Research or Clinical Team

Two Letter Site Code		Biobank Kit Code (Sticker) DO NOT include the TONiC study number
Site Name		
Date sample collected		
1) Check Kit Code matches Kit Label on consent form 2) Check all Kit IDs match on tubes and box		

Sample		Date Sample(s) Collected	Time Sample(s) Collected (HH:MM)
8.5ml SST serum blood	Collected: Y <input type="checkbox"/> N <input type="checkbox"/>	___/___/___	__:__
10ml EDTA blood	Collected: Y <input type="checkbox"/> N <input type="checkbox"/>	___/___/___	__:__
2.5ml Paxgene blood	Collected: Y <input type="checkbox"/> N <input type="checkbox"/>	___/___/___	__:__
Urine sample	Collected: Y <input type="checkbox"/> N <input type="checkbox"/>	___/___/___	__:__

**Archive the *Back* copy of this Part-A-completed form within the patient’s TONiC folder.
Include the *Top* copy of this Part-A-completed form with the samples when shipped to the Biobank.**

Comments:

Sample(s) collected by (Print Name):	Samples collected by (Signature):	Date: ___/___/___
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Part B – to be completed by the Biobank Team

Date Sample Received	___/___/___	Time Sample Received	__:__	Received by:
Sample	Confirm Receipt of Sample	Time of processing	Storage location	
8.5ml SST serum blood	Received: <input type="checkbox"/> Not Received: <input type="checkbox"/>	__:__		
10ml EDTA blood	Received: <input type="checkbox"/> Not Received: <input type="checkbox"/>	__:__		
2.5ml Paxgene blood	Received: <input type="checkbox"/> Not Received: <input type="checkbox"/>	__:__		
Urine sample	Received: <input type="checkbox"/> Not Received: <input type="checkbox"/>	__:__		

**For Biobank Team – Scan the completed form and email the copy to TONiC Team,
then file the original *Top* copy within the Biobank TONiC Folder.**

Comments:

Sample(s) collected by (Print Name):	Samples collected by (Signature):	Date: ___/___/___
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